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Title: Comparison of the protective effects of erythropoietin and melatonin on renal ischemia reperfusion injury in rats

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Introduction:

Ischemia (cessation of blood flow), followed by reperfusion, causes serious damage to tissues and organs [1, 2]. Ischemia compromises the continuous supply of oxygen required by tissues to survive and maintain physiological function. Ischemia of kidney is a common problem during kidney transplantation and partial nephrectomy leading to renal dysfunction and injury [3- 5].

Materials & Methods:

Under anesthesia, right nephrectomy was performed and then, the left renal pedicle was occluded by placing a microvascular clamp for 45 min to induce ischemia and then subjected to reperfusion for 24h.
The rats were divided into four groups:
The sham group (n=10) underwent only nephrectomy without occlusion.
IR group (ischemic control, n=10)
MEL + IR group (n=10)
EPO + IR group (n=10)
The blood samples and left kidney tissues of the rats were obtained after 24 hr of reperfusion in each group, the kidneys were removed and weighted. The blood samples were centrifuged at approximately 4000 g for 10 min at 4˚C. The urea and creatinine (Cr) levels in the serum were determined to assess the renal function.

Results:

Ischemia reperfusion significantly increased urea, creatinine, and decreased Hb and Hct values. Histopathological findings of the IR group confirmed that there was increase in hyaline cast and thickening of Bowman capsule basement membrane. Treatment with EPO or MEL significantly decreased urea level and increased Hb and Hct values. In the MEL + IR group, the histopathological changes were lower than those in the EPO + IR group.

Table 1 Biochemical measurements after 24 hr of reperfusion

	Sham group	IR group	MEL+IR group	EPO+IR group
Urea(mg/dl)	62.11±20.95	143.00±57.58[a]	102.37±17.91[b]	97.37±21.93[b]
Cr (mg/dl)	0.74±0.13	1.32±0.88[a]	1.14±0.20	0.93±0.21
RKW(% body wt)	0.38±0.03	0.41±0.04	0.42±0.05	0.43±0.06
Hct(%)	44.00±3.40	40.36±4.43[c]	46.10±3.66[d]	47.20±3.46[d]
Hb(g/dl)	14.66±1.13	13.45±1.48[c]	15.36±1.22[d]	15.75±1.10[d]

[a] Significantly increased when compared with sham group, P < 0.05.
[b] Significantly decreased when compared with IR group P < 0.05.
[c] Significantly decreased when compared with sham group, P < 0.05.
[d] Significantly increased when compared with IR group, P < 0.05

Cr, creatinine; RKW, relative kidney weight; Hct, hematocrit; Hb, hemoglobin; EPO, erythropoietin; MEL, melatonin; IR, ischemia reperfusion.

Results:(Continue)

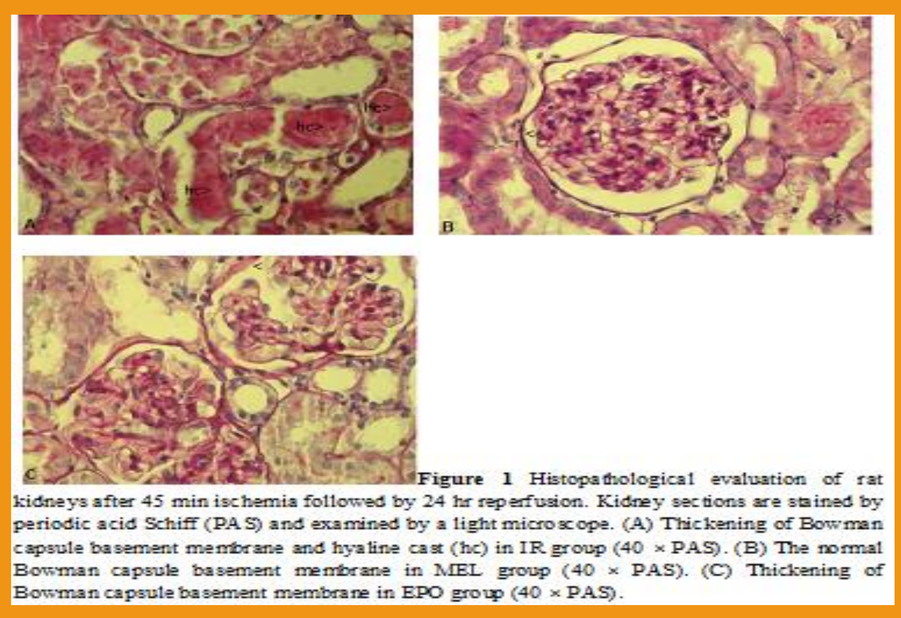

Figure 1 Histopathological evaluation of rat kidneys after 45 min ischemia followed by 24 hr reperfusion. Kidney sections are stained by periodic acid Schiff (PAS) and examined by a light microscope. (A) Thickening of Bowman capsule basement membrane and hyaline cast (hc) in IR group (40 × PAS). (B) The normal Bowman capsule basement membrane in MEL group (40 × PAS). (C) Thickening of Bowman capsule basement membrane in EPO group (40 × PAS).

Discussion:

ROS are considered to be principal components involved in the pathophysiological tissue alterations observed during renal IR. The administration of EPO and MEL, which are known antioxidant agents, appears to have beneficial effects on IR-induced renal injury as indicated by lower degrees of the histopathological changes and renal dysfunction. However, MEL pretreatment exerted more nephroprotective effect than EPO pretreatment, probably MEL was effective to reverse renal IR by its potent antioxidant effects. These results may indicate MEL protects against morphological damage better than EPO in renal IR injury.

References:

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